TRANSCRIPT OF PROCEEDINGS

DEPARTMENT OF HEALTH AND HUMAN SERVICES

FOOD AND DRUG ADMINISTRATION

CENTER FOR DRUG EVALUATION AND RESEARCH

GASTROENTEROLOGY AND UROLOGY DEVICES PANEL

OF THE MEDICAL DEVICES ADVISORY COMMITTEE

Pages 1 thru 239

Gaithersburg, Maryland
June 19, 2000

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Monday, June 19, 2000

10:00 a.m.

Gaithersburg Hilton
Salons D and E of the Ballroom
620 Perry Parkway
Gaithersburg, Maryland 20877

MILLER REPORTING COMPANY, INC.
735 8th Street, S.E.
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P A R T I C I P A N T S

Panel Participants

Anthony N. Kalloo, M.D., Chairman
Mary Cornelius, Executive Secretary

Voting Members

Jenelle E. Foote, M.D.
Joseph H. Steinbach, Ph.D.

Temporary Voting Members

Edward J. Baranski, M.D.
Patricia Smith Choban, M.D.
LTCDR Fathia Gabril, M.D.
Jules Hirsch, M.D.
Richard A. Kozarek, M.D.
John Linner, M.D.
Douglas B. Nelson, M.D.
Mark P. Sawicki, M.D.
Mark A. Talamini, M.D.

Diane K. Newman, R.N.C., M.S.N., Consumer Representative

FDA Participants

Jeffrey Cooper, D.V.M.
Dan Schultz, M.D.

C O N T E N T S

P R O C E E D I N G S

DR. KALLOO: Good morning, everyone. My name is Dr. Tony Kalloo. I would like to call to order this meeting of the Gastroenterology and Urology Devices Panel.

I would like to note for the record that the voting members present constitute a quorum, as required by 21 CFR, Part 14.

Would each member introduce him or herself, designate specialty, position title, institution and status on the panel, voting member or consultant, starting at my far right.

DR. SCHULTZ: I get to begin, thank you.

My name is Dan Schultz. I'm the Division Director for the Division of Reproductive, Abdominal and Radiological Devices. On behalf of the division, the office, the center and the agency, I would like to welcome all of you here, both panel members and guests and thank you for participating in this meeting.

DR. SAWICKI: My name is Mark Sawicki, an Assistant Professor at UCLA, in the Division of General Surgery.

MS. NEWMAN: My name is Diane Newman. I'm an Adult Nurse Practitioner in Philadelphia. I'm also a visiting professor at Rutgers College of Nursing and I specialize in urology and urinary continence.

DR. GABRIL: My name is Fathia Gabril, from NIH, Digestive Diseases Branch, Senior Clinical Investigator, Chief, GI Consult Service.

DR. KALLOO: Please state if you are a voting member or not, which you are.

DR. GABRIL: I'm a temporary voting member.

MS. NEWMAN: I am a consumer rep, non-voting.

DR. SAWICKI: I am a voting member.

DR. KALLOO: Thank you.

DR. STEINBACH: My name is Joseph Steinbach. I am a bio-engineer, bio-statistician at the University of California at San Diego. I'm a voting member.

DR. KALLOO: I will give Dr. Kozarek a second to get settled and then Dr. Choban, do you want to go first?

DR. CHOBAN: Patricia Choban, I'm a general surgeon and an Adjunct Professor of Human Nutrition at Ohio State and an attending surgeon for Bariatrics Specialist of Ohio. I'm a voting member.

DR. KOZAREK: Dick Kozarek, Chief of Gastroenterology, Virginia Mason Medical Center in Seattle, voting member.

DR. KALLOO: Tony Kalloo, I'm Associate Professor of Medicine at Johns Hopkins University and Clinical Director for the Division of Gastroenterology and I'm a voting member.

MS. CORNELIUS: Mary Cornelius, I'm a nurse consultant in the Urology and Lithotripsy Devices Branch and the Executive Secretary of this panel.

DR. TALAMINI: Mark Talamini, Associate Professor of Surgery, Johns Hopkins University School of Medicine, Director of Minimally Invasive Surgery there. I'm a temporary voting member.

DR. NELSON: Douglas Nelson, I'm an Associate Professor of Medicine, University of Minnesota Medical School and a Gastroenterologist at the VA Medical Center, temporary voting member.

DR. FOOTE: My name is Jenelle Foote. I'm a urologist in private practice in Atlanta, Georgia, where I am Clinical Assistant Professor of Urology at Emory and also in the Department of OB/GYN at Morehouse School of Medicine; voting member.

DR. HIRSCH: I'm Jules Hirsch of Rockefeller University in New York. I'm interested in obesity and nutrition. I am a temporary voting member.

DR. BARANSKI: My name is Edward Baranski. I'm a general surgeon from Gettysburg, Pennsylvania, retired. I'm a temporary voting member.

DR. LINNER: My name is John Linner and I am a temporary voting member. I'm a retired general surgeon. I am a member of the American Bariatric Surgical Society.

DR. COOPER: I'm Jeffrey Cooper. I'm a veterinarian in the Gastro-Renal Devices Branch at FDA. I will be taking over the Executive Secretary position from Ms. Cornelius at the next panel meeting.

DR. KALLOO: Okay, thank you.

I will now turn the meeting over to Mary, who will read the Executive Secretary's statement.

Mary.

MS. CORNELIUS: Good morning.

Before we begin, I would like to read a statement concerning appointments to temporary voting status.

Pursuant to the authority granted under the Medical Devices Advisory Committee, Charter for the Center for Devices in Radiological Health, dated October 27, 1990, as amended August 18, 1999 and November 16, 1999, Drs. Edward J. Baranski, Patricia Smith Choban, Fathia Gabril, Richard A. Kozarek, John Linner, Douglas B. Nelson, Mark P. Sawicki and Mark A. Talamini have been appointed as voting members by Dr. David W. Feigal, Director of the Center for Devices in Radiological Health for the June 19, 2000 meeting of the Gastroenterology and Urology Devices Panel.

Additionally, Dr. Jules Hirsch has been appointed as a voting member by Linda A. Suydam, Senior Associate Commissioner. For the record, Dr. Hirsch is a voting member

of the Endocrinology and Metabolic Drug Advisory Panel, Center for the Drug Evaluation and Research.

For the record, these people are special government employees and are consultants to this panel, under the Medical Devices Advisory Committee. They have undergone the customary conflict of interest review. They have reviewed the materials to be considered at this meeting.

The following announcement addresses the conflict of interest issues associated with the meeting and is part of the record to preclude even the appearance of impropriety. To determine if any conflict existed, the agency reviewed the submitted agenda and all financial interests reported by committee participants. The conflict of interest statutes prohibit special government employees from participating in matters that could affect their or their employees' financial interests.

However, the agency has determined that the participation of certain members and consultants and the needs for whose services outweigh the potential conflict of interest is in the best interest of the government. Therefore, waivers have been granted to Dr. Jules Hirsch, Richard Kozarek, John Linner, Patricia Choban and for their interest in firms that could potentially be affected by the panel's recommendation.

Copies of these waivers may be obtained from the agency's Freedom of Information Office, Room 12A-15 of the Parklawn Building.

We would also like to note for the record that, the agency took into consideration other matters regarding Dr. Jenelle Foote and Ms. Diane Newman. They reported interest in firms at issue, but in matters not related to today's agenda. The agency has determined, therefore, that they may participate fully in all discussions.

Lastly, we would like to note for the record that, Dr. Philip A. Schauer, who is an invited guest, has reported a pending involvement in the panel. Unfortunately, Dr. Schauer was unable to attend today due to a family emergency.

In the event the discussions involve any other products of firms not already on the agenda for which an FDA participant has a financial interest, the participant should excuse him or herself from such involvement and the exclusion will be noted from the record.

With respect to all other participants, we ask in the interest of fairness that all persons making statements or presentations disclose any current or previous financial involvement with any firm whose products they may wish to comment upon.

DR. KALLOO: We will now proceed with the open

public hearing session of this meeting. If there is anyone wishing to address the panel, please raise your hand and you may have an opportunity to speak.

I would ask at this time that, all person addressing the panel come forward to the microphone and speak clearly, as the transcriptionist is dependent on this means of providing an accurate transcription of the proceedings of the meeting.

Before making your presentation to the panel, state your name and affiliation and the nature of any financial interest you may have in the topic you are going to present. Each presenter has been allotted ten minutes.

The first speaker on the agenda is Brandi White.

[Pause]

DR. KALLOO: Yes, that would be fine.

Patricia McGraw.

[Pause]

PRESENTATION BY

PATRICIA McGRAW, PATIENT TESTIMONY

MS. McGRAW: My name is Patricia McGraw.

DR. KALLOO: Can we have a microphone to the podium, please.

MS. McGRAW: Hello, my name is Patricia McGraw and I am speaking as a patient.

DR. KALLOO: Please state if you have any

financial interests?

MS. McGRAW: No.

"Two roads diverged in a yellow wood and sorry I could not travel both and be one traveler, long I stood. I looked down one as far as I could, then took the other just as fair, because it was grassy and wanted wear."

Several years ago, I was at a crossroads in my life. At 31-years-old, I was 269 pounds and clinically obese, not to say I was diagnosed that way. You see, rarely if ever did I see a doctor. In fact, the mere thought of an annual physical was nothing less than a bad dream. Considering my family history and level of health risks, it was a foolish choice.

From a very young age to well into my 20s, I had attended more family funerals than most of my peers had been to in their lifetime. Practically the entire previous generation of my family was severely overweight and continued to suffer from heart failure, diabetes, stroke and cancer.

My father underwent a triple bypass surgery and continued to live with artery blockages until he died of a massive heart attack. My mother suffered high blood pressure and diabetes for as long as I can remember. She dropped dead of a stroke before she had the opportunity to meet and enjoy her grandchildren.

Why then would I, a young, well-educated mother of two avoid seeking medical attention?

I knew exactly how it would go. First, I would be told I had a weight problem, as if I didn't already know. I didn't need to be reminded about my high blood pressure. I thought of it every time I walked a flight of stairs. I didn't need to be told about my risk of diabetes. I thought of it every time I finished off a pan of brownies.

I absolutely did not need to be provided with a diet plan. You see, from Atkins to Scarsdale, I had attempted just about every diet on the market since I was 16 years old. I could have made up all the money I spent attending weight loss groups by writing a book of my own on the proper weights to even lose weight.

The difference was, I was never able to consistently maintain a program that made me feel good about myself. I was never satisfied and always frustrated. So, for nearly 15 years of my life, I felt like a failure and lived with poor self-esteem and lack of confidence.

The times I was forced to confront my lifestyle, I had a signature response. My mother died of a stroke. My grandmother died of a stroke. There's no reason to think I will be any different. I'm going to enjoy my life while I can.

Publicly, I maintained a pretty good life. I was

blessed with a wonderful husband who never mentioned my weight, two beautiful children who provided me with unconditional love and a career as a graphic artist. It kept me well hidden behind a computer terminal and, best of all, there was no dress code.

Privately, however, I was very often depressed. I spent long nights crying myself to sleep, too tired to enjoy my children in the morning. Most of all, I dreaded any occasion that forced me to go out and buy new clothes. It seemed every time I went to the store, I went up another size.

I was all too aware of my failure, but I honestly could not understand what seemed like simple, logical solutions to my weight problem. First, don't over eat. Well, I really didn't think I was. After all, once my stomach was bloated or I had to undo the top button of my pants, I stopped eating.

Second, only eat if you're really hungry. Well, since when does being hungry have anything to do with eating. After all, even after Thanksgiving dinner, there's always room for pie.

Third, eat healthy foods. Well, that's no fun. Looking back now, I realize I ate for comfort and a garden salad just didn't provide the same warm, fuzzy feeling of a brownie sundae.

One day, I brought my son to a friend's birthday party at a rollerskating rink. I watched from outside the rink, thinking of my own teenage years at rollerskating parties. Back then, I watched friends from outside the rink, too. I could stand on skates, but the fear of being the fat girl who fell trying to get up was more than enough to keep me from participating.

At my son's party I saw something else. Other mothers were actually skating with their sons. When my son asked if I could skate with him, my heart sank and I suddenly felt completely inadequate as a mother.

Coincidentally, it was around this time I heard of an acquaintance who had a gastric bypass performed. She was very close to my weight originally and was able to maintain a size that was previously unimaginable to me. So, after many months of soul-searching and investigation on the net, I decided to take the plunge.

I met with Dr. Rubenstein and his staff to discuss my options. After learning more about the gastric bypass and the VBG procedures, the risks seemed a little too drastic for my lifestyle. Then I was told about the studies being done on the LAP-BAND. Several considerations convinced me that this was the right procedure.

Laparoscopically, it was far less invasive to my body and because of that, I avoided the extended recovery

period I would have otherwise faced. As half of a double income household, having to scratch two months out of expenses, out of one income, would have been very difficult.

I also liked that the digestive tract stayed in use, as Mother Nature intended it to. Most interesting though was the flexibility it offered. Being able to adjust the opening of the stomach to suit my personal weight loss needs seemed to make so much more sense for long term success.

Dr. Rubenstein thought I was a good candidate, so I agreed to be a test case. Even though I was the first LAP-BAND procedure from our group, I actually felt more confident and less anxious going into surgery. So, 15 months later, I stand before this committee, having lost 97 pounds, over 45 inches and having gone down more than ten sizes.

At this point, you may want to hear about physical side-effects, problems or unexpected complications. Truth be told, I've experienced none of these. My procedure went smoothly. I was out of the hospital in 18 hours and back to work in only two weeks. I have had two adjustments to restrict the passage of food. Both were quick, painless and uneventful.

One of the many reasons I selected Dr. Rubenstein to perform my surgery was the follow-up group that his

practice offered. I felt at the time and still feel very strongly that, the group support of those who have walked the proverbial mile is vital, not only in making the decision, but in staying focused on the road to success and helping to regain lost self-confidence.

Ironically though, the group I had relied on for support made me feel even more uncomfortable for having such a successful and unencumbered recovery and weight loss. I found that those of us who had the LAP-BAND procedure were far more concerned with psychological issues than patients who had procedures, who had other procedures, who seemed to be enduring very difficult physical struggles.

After the physical recovery, I quite literally had to relearn how to eat and treat food and I'm still learning. The follow-up group uses the term fat brain. This muscle is far more difficult to restrain than the stomach. Although other types of weight loss procedures force the patient to reevaluate their mental association with food, I believe that because the LAP-BAND is so significantly less disturbing to the body, it allows more energy for the mental recovery and the mental focus that is needed for long term success.

It took some time and a lot of that focused energy to realize that, just because food smelled good or looked inviting, did not mean I needed to over eat it in order to

enjoy it. I have changed on the outside, but the more important changes are still happening on the inside.

This presentation to you would not be complete if I failed to have you understand the importance of not only the weight loss, but of shedding the idea of living my life based on a preconceived death sentence. Although significantly reduced, I am still aware of my health risks through the family history. For the first time in my life, I no longer live with resignation and excuses. Instead, I am empowered to make better choices and take control of my own destiny.

Food is no longer a source of entertainment and comfort. Now, I get pleasure from kick-boxing three times a week and walking one to two miles a day. I actually feel bad mentally and physically when I don't work out. I was never a shy person, so I won't tell you my weight loss has brought me out of my shell, but it has given me the self-confidence to take a stand and be heard on more serious issues and worry less about what other people will think of me.

In my professional career, I've come out from behind my computer terminal. I played an integral part in labor relations for my company and have recently accepted a promotion as shift supervisor. On a more personal level, I've discovered a lot about myself over the past year, but

discovering a new muscle group is something I previously would have never thought an exciting moment in my life.

I share a hug with my husband everyday and for the first time, I feel his arms go completely around me. Most thrilling of all though is that, now, instead of just watching my children play, I'm able to get up and play alongside them.

I will not have good childhood memories revolve around where we used to go for good dinner. Instead, I have chosen to provide them memories of walks in the park, riding bikes and, yes, maybe even some day rollerskating together. Instead of sharing a favorite food, we now share the same martial arts instructor.

I'm quite certain that Robert Frost never intended such a correlation, but I can't help but make his own words my final words to this committee.

"I shall be telling this with a sigh, somewhere ages hence. Two roads diverged in a wood and I took the one less traveled by." But that has made all the difference.

Thank you.

DR. KALLOO: Thank you, Ms. McGraw.

Brandi White?

Not ready yet, okay.

Dr. Martin?

PRESENTATION OF

LOUIS MARTIN, M. D.,

CLINICAL EXPERIENCE, EXPLANTS AND CONVERSIONS

DR. MARTIN: I have slides if they can be put on.

I'm sorry, this is my fifth presentation in a week. We had a meeting last week of our professional society.

DR. KALLOO: Could you tell us your name and affiliation, please? Thank you.

DR. MARTIN: Dr. Louis Martin, I'm a Professor of Surgery and Public Health and Preventive Medicine at LSU in New Orleans. I have been one of the investigators in this study and put in the largest number in the two trials, but I have no stock or other financial considerations related to the company. I do expect to benefit if the device is approved.

I did give a copy of my slides, because I have some figures here. I apologize for not having them in advance, but I will try namely just to speak.

I was asked mainly by my patients to come here. This new device is changing practices in our bariatrics surgery community, just as laparoscopic surgery is changing the number of patients that come and our experiences in our practices. I felt it was important, just because we are a very divided group right now in the obesity-surgery market to express what I felt my patients' concerns were about the

individual roads that you are going to hear several patients and the rest of us talk about.

There are different people coming to us because of this band that would not have come to us otherwise. They are bringing us new ranges of problems that have to be considered.

Specifically, I am also the person who has explanted the most patients. I have nine patients that, after variable periods of time, from one year to three years, have decided that their weight loss was not adequate enough and they have been converted.

I was hoping this would be on one slide, but it is not.

A third of them in the first year, a third of them in the second year and a third of them in the three years, the third year, so it is a very individual process that they struggle with. They have basically more than doubled their weight loss after the conversion from approximately 12 percent to approximately 30 percent of total body weight, making it effective but not as effective as my gastric bypass patients.

Many of them stuck with it, as you can see, for three years. They really wanted this to work, but when it did not, they did want to convert. More significantly, two of the patients, after conversion, went into severe

psychological distress for up to six weeks, because they were able to gain the band and they were not able to gain the gastric bypass. So, the people, I think, who come to this, come with a different set of expectations, a somewhat different psychological profile and our practices have to adjust.

That has been one of the problems. I think some people have given up on the band because the practice with the band is different. Your staff and your on mindset has to adjust.

Next, I have had nine percent of patients that have to be converted to a gastric bypass. There are four extra patients on this slide, two others that I had to participate in their conversion, one from the second study and one from Dr. Kuzmak's [ph], an initial group of patients in 1991, plus two of my own patients who asked to have the band removed and did not want a conversion to gastric bypass.

So, that is nine percent due to obstructions and four percent that did not want to be converted.

The big thing, again, on this slide is, I wanted to figure what happened because, again, some of these conversions and obstructions are devastating and this slide is not projecting well.

First, Dr. Kuzmak's patients who is over nine

years after a gastric bypass and who did not have an adjustable gastric bypass, came in, referred to me three years after not having seen a doctor with an esophagus that was bigger than a colon. She had been sleeping in a chair for two months before she sought medical attention. She had a severely obstructed esophagus. She was converted relatively easily, but because we did the conversion rather than take the band out, we didn't have the perfect sterile situation and she developed a wound infection.

Another patient of a friend of mine in San Diego that did the same thing, wound up with an atonic pouch essentially, after having an obstruction due to the band. This is a problem we don't quite know what to deal with.

In my own group of conversions, two of them were easily done laparoscopically, one due to a woman who had to start taking a large number of pills for chemotherapy that would not go through the obstruction. One of my patients that was an easy conversion, four years after the band, died on the first postoperative day, weighing a hundred pounds less than she did in her initial operation, at a weight where she was now only 50 percent above ideal body weight.

So, these things always take us back and I think there is still quite a bit of learning we need to do before we know how exactly to use this.

Finally, I have had to convert four patients due

to infection. This is an implantable medical device.

My most interesting story is, I had a woman who was very successful. In her fifth year was attacked on the job and developed an infection at her port site and had to be converted. So, you're never out of risk with this subcutaneous device setting there. She's had a problem because the infection was treated under workman's comp and we had to deal with it for six months before they gave us permission to convert her. She has developed a stricture with inflammation. In treating her with steroids, I gave her a neuropathy for a while.

The second patient developed an infection at the port site when a plastic surgeon did a panniculectomy and infected the access site, not paying enough attention. My third patient eroded three years after the band was placed, not knowing quite why she eroded. The final patient was due to a technical error. When we put the band in the first time, we perforated the stomach and didn't realize it. We found this two months later. She has been converted to a gastric bypass and has done well.

The biggest thing I wanted to talk about, because it is not part of the other presentation is, how easy is it to convert or removed the band. What we found is, most removals can be done laparoscopically, especially if we did the whole experience. In the total study, 17 have been

removed laparoscopically versus 12 open.

Many revisions and a few conversions can be done laparoscopically, especially as we get better. That has been one of the best elements of this protocol for me. I was not a great laparoscopic surgeon beforehand. Now, I do 90 percent of my gastric bypasses laparoscopically. In our early experience, only three of 12 revisions were done laparoscopically. Most recently, six of ten revisions have been done laparoscopically and, as I said, I've been the only one able to convert a gastric banding to gastric bypass and I have done three of them.

Our highest complication rate seems to be when conversions are done due to an obstruction. We still don't know quite whether we are going to have to do this always as a two stage procedure or what conditions we will be able to do it simultaneously.

In conclusion, does the LAP-BAND fill a gap in our practice?

Well, none of my patients initially wanted a gastric bypass. They all used words like mutilation and irreversible when we talked about a gastric bypass, even though I still consider that a far better procedure from an effectiveness. So, this brings a new group of people to practice who will have an effective therapy. We have been able to do our conversions.

Talking to people about what operation they should have, it is interesting that one of our patients who was not a sweet eater became a sweet eater. All of our patients who thought they would use the LAP-BAND did learn to work around it.

In the problem area, I have had two major psychological complications with conversions. So, I do think this is a different patient population we are dealing with. We need to continue to refine selection criteria and I don't think we can do that until it is more widely available.

However, on the plus side, two others who had major psychological problems that we knew about that avoided them while they had the LAP-BAND in were able to embrace counseling after the conversion with our help and the process they went through.

Thank you.

DR. KALLOO: Okay, thank you, Dr. Martin.

Brandi?

MS. WHITE: Hi, I'm Brandi White and I don't have any money and they don't owe me any money. I'm just hear as a patient. Is that what I need to--I'm not a public speaker, obviously.

[Pause]

DR. KALLOO: Should we skip ahead to the next

speaker or--

MR. LINDSTROM: We are ready.

DR. KALLOO: You're ready? Okay.

[Pause]

PRESENTATION OF

WALTER LINDSTROM, ESQUIRE,

OBESITY LAW AND ADVOCACY CENTER

MR. LINDSTROM: Okay, I'm sorry.

Good morning. My name is Walter Lindstrom, of the Obesity Law and Advocacy Center. I have no financial interest in this decision today.

I have requested the opportunity to present my viewpoint to the committee and urgently hope, for the reasons I discuss today and for the future information you hear, that you will enthusiastically recommend approval of the LAP-BAND. I believe that my perspective and the opinions of the hundreds of persons whom I represent will convince this group that, such an option for the surgical treatment of morbid obesity is absolutely imperative and to delay its availability will be contrary to the needs and desires of literally millions of persons who are suffering from this disease.

On March 1, 1996, I founded the Obesity Law and Advocacy Center, the first to date only private law firm in this country, based out of San Diego, solely dedicated to

representing the interests of persons suffering from the diseases of obesity and morbid obesity. During the four and a half years of this practice, I have personally represented almost a thousand clients in every state in this country, all of whom have sought surgical intervention for their morbid obesity. My practice specializes in handling claims against insurers, HMOs and self-insured entities who wrongfully deny access to what is considered by the National Institutes of Health as the single most effective long term solution for their disease.

My professional involvement in this matter transcends the individual clients and their cases. I have been honored to prevent lecturers on many legal topics related to morbid obesity and to access treatment with respect to unfair and illegal discrimination against the morbidly obese. I have worked with professional organizations, such as the American Obesity Association, the American Society for Bariatric Surgery, the American Society of Bariatric Physicians, NASO, and many other similar organizations with allied interests. I have addressed state and national legislators on topics involving managed care and morbid obesity treatment and I have worked to assist persons in Georgia, Indiana and Virginia in passing legislation to increase access to the surgical treatment of morbid obesity.

In addition, I participate in a number of Internet-based support groups who work together as a community to battle this tragic disease. As an obesity rights advocate, I feel comfortable saying to this committee, without exaggeration, that my practice and the work that has been done has established me as one of the leading consumer and patient voices with respect to obesity issues in general and, in particular, with respect to obesity surgery.

My interest in this topic is not merely professional. It is deeply, deeply personal. I, too, have experienced the torment of living as a person of size in this country. I, too, have experienced the health risks and substantial limitations in major life activities that morbid obesity creates. I, too, have experienced the syndrome of trying any proven or unproven intervention in the hopes that, this time, it might work.

I have been on fasting programs where I have not eaten solid food for ten months. I have taken drugs and been on every conceivable diet.

On June 30th of 2000, I will celebrate the six year anniversary of my own bariatric surgery. At the time of my highest weight, I was 400 pounds. I wear this button as a remembrance of where I have been, but also as a way of demonstrating to my clients where their road to treatment

might lie if they get their access.

My surgical procedure was a gastric bypass and, while I am pleased to have maintained the results that you see, I will tell you in all candor, had the LAP-BAND been available to me at the time of my surgery, unequivocally it would have been my first treatment of choice. Now, it is time for this committee to pave the way so that the clients I represents and the persons I serve who suffer from morbid obesity have this option available to them.

I have come here at my own expense from San Diego because I am of the deep and abiding belief that, approving the LAP-BAND is integral to an overall battle that this country is facing with morbid obesity. The clients that I represent are all seeking a safe and permanent tool to assist them in managing and treating this chronic disease. Many of them, for very valid, personal reasons, are afraid of the majority of bariatric surgical procedures that are currently utilized. The LAP-BAND is an answer to the prayers of many who fear these more invasive procedures.

The gastric bypass I had is essentially a permanent re-arranging of my gastrointestinal system and is a procedure that scares many of the clients that I represent. It is a procedure that is to some so frightening that they would choose to live with the horror of this disease rather than to seek intervention.

The LAP-BAND offers to persons suffering with this disease, the people that I represent, a truly minimally invasive surgical tool to manage their illness. As part of the work that I do and part of the practice I have, I have read much of the literature concerning the successes, failures and complications of this procedure by investigators involved in this trial as well as the European surgeons who have utilized this practice for many, many years. I have been fortunate to discuss this procedure directly with doctors from Europe and Australia and from all over the world who utilize this as the primary tool and their ally in the fight against morbid obesity.

This device offers one possible solution to those of us who are suffering. It is safe and effective and should be readily offered and available so long as the surgeon using the device is properly trained and is committed to the care needed to be a competent bariatrics surgeon.

This committee will, no doubt, hear from some out there, including surgeons who specialize in bariatrics surgery that, will state that the data does not support the LAP-BAND as being an as effective operation as the operation I have. My answer to those skeptics is quite simple.

We can all agree today, at the beginning of this meeting that, this is not a perfect procedure. I have never

seen in my work as an obesity rights advocate, whether it is medical therapy, dietary therapy or any other type of therapy, the perfect procedure that is out there. To criticize a procedure for its lack of perfection is disingenuous at best and motivated by self-interests at worst.

The fact is, this procedure is an extremely effective tool for person who utilize it properly. It is minimally invasive and offers a real chance at managing one's disease without altering one's anatomy. It's a chance I wish I had six years ago. Many of my clients want that chance now and I hope this committee will give it to them.

In September of '98, NIDDK and NHLBI published this nation's first clinical guidelines on the identification, evaluation and treatment of overweight and obesity in adults. The report generated by NIH detailed that there were multiple treatment modalities available to treat this chronic disease, including the ones that I just mentioned and pharmacotherapy as well. These are talked about as alternative treatments and the LAP-BAND clearly should be one of those treatments made available in this continuum of treatment modalities needed to affect this disease.

There are persons with proper evaluations who shouldn't be candidates for the LAP-BAND, but that is true

for all surgical procedures. That has to be done at the judgment and discretion of the surgeon properly trained to evaluate their patients as to whether or not this device should be implanted. That is training that I believe bariatric surgeons are capable of doing.

In closing, unless you suffer from this disease, you cannot truly appreciate the magnitude of the decision with which you are confronted today. You cannot imagine what it is like to live in a country where you have to survey your surroundings for a safe place to sit. You don't have to go outside because the kids make fun of you. You choose not to go to your parent-teacher conference or to the open house for your kids because you don't want your child to be subjected to the torment of other kids making fun of them because mommy and daddy are so fat.

You cannot imagine how important your decision is to the people you will never see or talk to, but the ones that I represent everyday. They are looking to me for some hope that they can access safe treatment, as advised by their doctor. I turn to you to give them that hope.

I want to represent my report to my clients and others who see me, for whatever reason, as the only voice they have in fighting this battle; that this committee and the FDA is going to provide them with another weapon in their arsenal to fight this epidemic. I want to be able to

report to them that, if they fear having their anatomy disrupted, there is a worthwhile option for them and they have a tool they can use with confidence.

I want to go home and tell the people I represent that they have another chance to fight this chronic disease that robs us of our quality of life, that devastates our families and that causes us to die too soon. I want them to be able to play with their children and grandchildren and have the quality of life they deserve.

For some, for many, the LAP-BAND offers that chance at a quality of life. Please give me something good to tell them when I get back home. I have so many people counting on me and now I'm counting on your.

Thank you.

DR. KALLOO: Thank you, Mr. Lindstrom.

Okay, Brandi White is going to try again.

[Pause]

DR. KALLOO: Should we move to the next speaker?

[Laughter]

MS. WHITE: This doesn't count as part of my time, does it?

[Laughter]

[Pause for set up]

DR. KALLOO: Looks like we're getting close. My VCR at home also has a flashing 12 o'clock.

[Laughter]

[Pause for set up]

DR. KALLOO: Why don't we continue and just hold off. Hopefully, the last one will be a charm.

The next speaker is Lynn McAfee, please.

PRESENTATION OF

LYNN McAFEE, DIRECTOR OF MEDICAL ADVOCACY,

COUNCIL ON SIZE AND WEIGHT DISCRIMINATION

MS. McAFEE: I'm Lynn McAfee. I'm Director of Medical Advocacy, for the Council on Size and Weight Discrimination. The council is a non-profit group that does not accept money from the weight loss industry.

DR. KALLOO: Can you just turn it off for now, please? Thanks.

MS. McAFEE: Don't lose your place on it.

DR. KALLOO: Could you also mention if your travel costs were reimbursed as well by the company?

MS. McAFEE: No, we don't accept anything.

This is the seventh advisory meeting I have attended. The first six were Edican and the committee meetings on diet pills. As I discovered in those meetings, it is hard to comment intelligently on these things, before one sees some company's data presentation. So, my remarks today will be of necessity quite broad.

First, I would like to talk about the idea of

obesity as a disease and the obesity epidemic. By the way, it has been medicalized only in the last few decades. The idea of a fat epidemic is even more recent.

I have spoken to medical sociologists and medical anthropologists and to bioethicists and none of them believe obesity should be technically and legally a disease. What they explained to me is, that disease and epidemic or social terms and not medical terms and not quite precisely defined, therefore. The increasing number of conditions labeled disease in the last few years reflect both social and economic motivations.

Socially, the disease label removes the stigma of volunteerism. We are viewed as victims of a condition we didn't create. When we have a chronic condition, we are always in treatment, always in need of help from the medical establishment. Disease terminology may make people think of you more sympathetically, but they also think of you as inferior to them and needy. We are put in what one disabled author called a liminable condition. We are viewed as somewhere between child and adult, not fully vested in our responsibilities or our rights.

Economic reasons for the disease label have to do with the health care system in this country. If it is not a disease, in short, we won't pay for treatment. Treatment is not available then. If it is a diseases, it also gets more

NIH funding. If it is a deadly disease, then even treatments with high failure rates will be tolerated.

Obesity is not leprosy and it is not--we don't live in a strictly disease and not diseased world anymore anyway. Behavioral geneticists have located the gene for shyness. Is shyness now a disease?

We need a new paradigm for conditions at the intersection of biology and environment. We are not well-served by attempts to make body weight a disease. I'm not arguing that fat has no health risks. There are considerable health problems associated with this, far from the case that they are not problems.

My point is that, words like disease and epidemic often skew the risk-benefit analysis by their emotional impact and the primal fear they raise. It's tempting to try anything to stop an epidemic. So, treatments with great risk and little effectiveness can be perceived as a reasonable response to what is also perceived as a desperate medical situation.

Yet, although obesity is linked to and, perhaps, causative of diseases like diabetes and hypertension, there are conflicting reports on how successful sustained weight loss is because no launched study has ever been able to keep weight off long enough to know whether there are real health benefits from weight loss. It is for this reason that the

NIH is beginning one of the longest trials in its history, the SHOWL trial, Studied Outcomes of Weight Loss.

One thing that has never been satisfactorily addressed and that we hope will be shown in this trial is, are our morbid conditions left worse off when we regain weight than if we had never lost it. Amazingly, we don't know and because of the failure rates of these operations, that is an important issue for us here today.

What little we know about sustained weight is coming out of the Swedish Obesity Study, SOS and even that data is problematic. The failure of gastric restriction weight lose surgery is quite high. So, the pool of people who sustain weight loss is much lower than had been anticipated for a study. Even more troubling, some of that data appears to show that, even when weight loss is maintained, initial improvements of hypertension begin to degrade after about three years and return to baseline.

Weight loss is desirable for a number of health reasons. The issue is, does the LAP-BAND deliver that sustained weight loss? I hope so, but I'm not optimistic.

Recent reports on the vertical banded gastroplasty show that long term failures are more than common. At a ten-year follow-up, it was reported that only 23 percent of patients after VBG retained a weight loss of at least 50 percent. Twenty percent had to undergo reoperation.

Will the LAP-BAND succumb to the same problems as a VBG and the gastric bubble? Will the stomach merely stretch dramatically to accommodate more food? Will initial weight losses be eroded over time? The natural history of this disease is a long one. We need at least five to ten years to really know this.

The LAP-BAND appears to have considerable advantages over other restrictive operations: lower reoperation rates, less surgical trauma, less invasive, more easily reversed and, hopefully, less postoperative infection. As the reigning queen of postoperative infection, that is an important issue to us.

Indeed, to a layperson like myself, this seems like a cross between a VBG and a gastric bubble. Will pumping up the volume really be successful? In reality, the LAP-BAND will probably use an operation that will both restrict gastric size and be malabsorptive. In fact, earlier this month bariatric surgeons went to the NIH Task Force on Obesity meeting and requested another consensus panel on weight loss surgery be convened next year to improve these restrictive end malabsorptive operations, so the insurance companies will pay for them more readily.

This operation that we are looking at today has one thing in common with Redux and Phen-Fen. It is really based on old science, the old paradigm for obesity. It

concerns itself with hunger and satiety and it views these concepts simplistically as coming exclusively from the stomach. We know that hunger and satiety are very complex manifestations of a series of chemicals, some of which go directly from the (?) site to the brain. The stomach itself is more than just a feedbag that can be easily fooled into thinking it is full of nutritious food.

My friend, Nigel, who had weight loss surgery twice, once said to me that the worst part of the surgery was always being hungry and never being able to extinguish that hunger. This certainly is not everyone's experience, but the comment was not unique. So, our major concern is effectiveness. As to safety, because this is laparoscopic, we assume that peri-operative mortality and infections rate will be much improved over the older surgeries. The stomach is not nearly so mutilated, and this is a big advantage.

Although a recent study with the LAP-BAND showed no adverse results to fetuses in 18 women who became pregnant after banding, the periods of starvation in Europe, in World War Two, have showed that children conceived during times of severe caloric restriction may pay a price later in life as obese adults.

We would also like to be reassured that the LAP-BAND will not, like the gastric balloon, dislodge and present potentially life-threatening problems. We have seen

some people develop serious vitamin deficiencies and we would like to be reassured regarding that issue. This is a particular concern in the restrictive and malabsorptive operations.

I might say, having spent two days listening to Xenical presentations, I'm very concerned about what little is known about vitamins and about the chronic deficiencies in vitamins that obese people suffer to begin with.

Perhaps the main reason people in this country get weight loss surgery is social and not medical. To be fat in this country is to live a second-class life, cut out of opportunities others think of as their birthright, subject to scorn and abuse of all kinds because of our body size. We are considered aesthetically inferior, a notion I reject.

Of course, losing weight will remove our stigma, but I must say that I strongly object to quality of life scales that use as reduction of stigma as a justification for any weight loss method. Doing so gives tacit support to a pervasive social prejudice and that is not an acceptable solution to a social problem.

Finally, let me say that, it is my hope, my sincere hope that my concerns today are groundless. I am a person who is disabled by my size, facing life-threatening illnesses related to my size. No one will be happier than me if I hear today evidence that shows the LAP-BAND to be

effective and safe. Weight loss surgery has too often been unreasonably exuberant about new surgeries and stubbornly blind to their failures.

Patients routinely should a hundred percent of the blame for their failure to maintain weight loss. Today finally, the surgery will be evaluated upon its own merits.

Thank you in advance for your efforts on our behalf.

DR. KALLOO: Thank you, Ms. Lindstrom.

Okay, let's try this one more time, Ms. Brandi White. Can you start again and reintroduce yourself?

PRESENTATION OF

BRANDI WHITE, PATIENT TESTIMONY

MS. WHITE: Yes, I sure can.

I'm Brandi White and I'm a patient, LAP-BAND patient and I'm six months pregnant with twins. So, I will not be speaking on safe sex today. We have a 3-minute video. And nobody gave me any money to be here and they didn't pay for my train ticket.

Yes?

DR. KALLOO: How long is your video, I'm sorry?

MS. WHITE: Three minutes.

DR. KALLOO: Three minutes, okay, very good.

MS. WHITE: Thank you.

[Videotape shown]

MS. WHITE: Thank you.

Why am I here today? I am here because there is not a product that I believe in more than the adjustable LAP-BAND.

As I said, I am pregnant with twins and we're very excited about that. When I was 305, my menstrual cycle had stopped and the doctor told me the likelihood of me, if I was to ever get married, the likelihood of me ever having children would be zip. So, I believe it has been a real miracle.

What is it like to be 305? It's miserable. I would just challenge anybody on this panel to go and buy three 50-pound bags of cement or three 50-pound bags of dog food and take them to your body and walk around in our society for one day with an extra 150 pounds.

How would you feel? You would be sweaty. You would be tired. You would be--your feet would hurt. It would be hard to move. It's hard to breathe. I do believe it's a disease. I believe it's a disease of the body and of the soul and of the spirit. It is the worst kind of disease, as far as I'm concerned.

I remember going to a soccer game with my nephew and he was so excited that I was there to see him play in his first soccer game. I could not fit through the gate. They put a bar up because high school kids were driving

through there and they put a bar up to prevent motorcycles and everybody was going in and I couldn't fit through the gate. That's disgusting. That is no way to live.

Why couldn't I lose weight? I'm not sure. I had had limited success--I need to make a correction on the video. I kept my weight off for two years, until I got pregnant and then we loosened the band so I could gain weight. I have done that also very successfully.

Why couldn't I lose weight before? I'm not sure. I had tried everything. Everything Oprah had been on, I had been on. My parents sent me to fat camps. I hired a Jamaican doctor. He came down and would beat the fat off me and it stayed. I'd have to drink these herbs. I was just desperate. I was desperate.

I've enjoyed "Big is Beautiful" and you know, it is not. The only place I was ever accepted, weighing 305, was when I was on a mission trip to Guatemala and we were in the jungle. We had gone into this small, small village and they had never seen a medically-obese person. So, they thought I was a queen and they all ran up to me and started squeezing my fat.

Well, I don't want to live in the jungle, in Guatemala. I want to live here, in the good old U.S. of A. It was a nightmare, moving, breathing. At the grocery store, people would come by and look at my basket and look

at me with disgust, even if I just had healthy food. A man even took something out and said, you really don't need this.

I don't think you realize what it is to live like an obese person in the United States until you have done it. People would say to me just stop eating, exercise. If I could have done that, I would have. If I had that power, I would have done it. I'm not sure why I didn't. I don't know if I have the fat gene or whatever. It didn't matter.

What mattered was that, I was obese and I was discriminated against and I was miserable.

My life changed three and a half years ago when I had the LAP-BAND. I did not starve myself. I would be full and I remember my first meal after my surgery and I felt full. I thought to myself, this is what it is. You know, when people say, oh, I'm so full I'm about to pop. I had never felt that. I could always eat more. In fact, I never felt satisfied. I remember the first time feeling full and it was a wonderful, wonderful feeling.

I believe in this product so much that, as you saw, I had my sixty-year old mother--I'm not supposed to say her age. My mother had the surgery and she's already lost weight. I have sent 15 others to have the surgery and they have all lost weight. Probably the most important person in my life was my priest and, being a very religious person,

you don't have a priest do something that's going to cause you any kind of trouble.

[Laughter]

MS. WHITE: I sent him to have the surgery and he has lost 80 pounds.

Please, please, please pass this for those who suffer. If you don't think we discriminate against fat people in this country, tell me your first thought when you're on an airplane and a large person gets on the airplane and you have an empty seat next to you. We all do it. When a large person gets on the plane, our first thought is, oh, God, please not next to me. We discriminate; we do.

Now, there is hope and there is a problem that we have and we have something that can fix it. It did in my case and many others.

Thank you.

DR. KALLOO: Thank you, Ms. White.

Next is Morgan Downey.

PRESENTATION OF

MORGAN DOWNEY, ESQUIRE,

EXECUTIVE DIRECTOR AND CEO OF THE

AMERICAN OBESITY SOCIETY

MR. DOWNEY: Good morning.

My name is Morgan Downey. I have no AV

requirements.

I'm a person with obesity. I am the Executive Director of the American Obesity Association. We do receive financial support from several companies in the obesity treatment area, including Hoffman LaRoche, Knoll Pharmaceutical, Amgen and Weight Watchers. We do not receive any financial contribution from the sponsor of this device.

AOA was founded in 1995 as an advocacy organization for the interests of millions of persons in this country with obesity or risk of obesity. Our interests include expanding research on obesity, encouraging programs for prevention, expanding knowledge about obesity, improving treatment and access to them, policing consumer fraud in the weight loss industry and overcoming stigma and discrimination directed against persons with obesity.

Obesity is a chronic disease. It is responsible for approximately 300,000 deaths per year. To find as a body mass index of 30 or greater, obesity has increased from 14 percent of the adult population in 1996 to 22 percent from 1998 to '94. Thirty-seven states have obesity rates higher than 15 percent. In 1991, that number was only four.

According to authors from the Centers for Disease Control an article and actually a whole issue devoted to obesity in "JAMA" in October of last year, these data

regarding the increases in obesity show that, obesity increased in every state, in both sexes, across all age groups, races, educational levels and smoking statuses. The authors state: Rarely do chronic conditions, such as, obesity spread with the speed and dispersion characteristic of a communicable disease epidemic.

Obesity is strongly associated with many comorbid conditions. Several are very well established, include type II diabetes, gallbladder disease, coronary heart disease, high blood pressure, high cholesterol, sleep apnea, pulmonary dysfunction, stroke, liver disease, reproduction dysfunction, several cancers and osteoarthritis.

According to a recent article from the National Institutes of Health, National Task Force on the Prevention and Treatment of Obesity, quote: The data linking overweight and obesity to adverse health outcomes are well established and incontrovertible. Most studies show an increase in mortality rate associated with a BMI of at least 30. Individuals with a BMI of at least 30 have a 50 to 100 percent increased risk for death due to all causes, compared with individuals at a BMI of 20 to 25, with most of the increase due to cardiovascular causes.

According to a study performed for AOA by the Lewin Group last year, obesity is responsible for approximately $102 billion in direct health care expenses in

1999. Health care utilization and health care costs correlate with increases in body mass index. One study, not the one we commissioned, another one found that the cost to U.S. businesses of obesity was 2.6 billion for mild obesity, but nearly five times that much for moderate to severe obesity.

Severe obesity, which we define as a BMI of 40 or greater, is a major public health problem. Patients face not only the prospect of premature death, but suffer usually with more than one comorbid condition. In addition, many patients deal with serious psychological disorders, including depression or binge eating disorder, poor quality of life, above average lost days of work, employment discrimination and numerous humiliating exposures to expressions of stigma, which you have eloquently heard from previous witnesses this morning.

Obesity surgery has an important role to play in the treatment of obesity, which has been recognized by public and private health organizations, including AOA and the National Institutes of Health. Indeed, it is often a life saver. Many persons look at obesity surgery when all other weight loss approaches have been tried unsuccessfully and are concerned about staying alive.

In our office, next to calls about childhood obesity, the largest number of calls seeking information

come from persons considering obesity surgery. We are, therefore, excited about the prospect that a new procedure may be available, which provides an additional therapeutic approach. Obviously, it is the responsibility of the FDA and this committee's advice to determine if the device under consideration meets established safety and efficacy standards. Assuming the device can meet those standards, we would urge that the device meet three criteria.

First, providers of the service must be appropriately trained, both in the surgical technique but also in understanding pre and postoperative psychological and social needs of their patients.

Second, adequate follow-up of these patients must be assured.

Third, to prevent abuse, precise criteria for patient selection must be in place.

Should these standards be met, we would hope that the Food and Drug Administration would move quickly and expeditiously to provide persons with severe obesity one more alternative therapeutic approach.

Thank you.

DR. KALLOO: Thank you.

Our next speaker is Dr. Harvey Sugarman. Is he here?

[Pause]

PRESENTATION OF

HARVEY SUGARMAN, M. D.

VIRGINIA COMMONWEALTH UNIVERSITY

DR. SUGARMAN: My name is Harvey Sugarman. I am a Professor of Surgery at Virginia Commonwealth University in Richmond, Virginia. I was the principle investigator at our site for the evaluation and use of this device. In that regard, BioEnterics did support a nurse clinician who worked with these patients in the process of the evaluation and use of this device.

I and my two colleagues who performed the operation--

DR. KALLOO: I'm sorry, could you state if you have any affiliations with the company?

DR. SUGARMAN: I just was saying that, the affiliation was that, we were one of the centers supported by BioEnterics.

DR. KALLOO: I see.

DR. SUGARMAN: I have come here on my own, though, and I have paid for my transportation.

My concern and reason for presenting today is that, early approval of this device prior to the full three-year follow-up that was originally agreed to by BioEnterics and the FDA might be reasonable if the device had no problems and if the results were excellent. But we have at

our center and several other centers concerns about the safety and efficacy of this device.

As a result of the FDA trial, it was mandated that patients undergo an upper gastrointestinal barium study to evaluate the band after its insertion and as a consequence, because of that mandate, we found a significant percentage of our patients who developed a dilation of their esophagus above the band. So, complications of the LAP-BAND include infusion port problems, stomal obstruction, as you have heard, erosion of the band into the stomach, slippage of the band and the need for its being repositioned, dilation of the pouch above the band and esophageal dilatation.

We had 38 patients entered into the trial of whom we were able to successful place the band in 37 patients. In this group we had complete data on 25 patients with preoperative and follow-up upper GIs in these individuals. This is an example of a preoperative upper GI and we sized the esophagus by comparing it to the vertebral column.

This is two years later, showing fairly significant dilation of the esophagus above the band, which is placed on the stomach and not on the esophagus, in this instance, although we were asked to place the band higher and higher because of problems with band slippage.

This is another postoperative upper GI in a patient with significant esophageal dilation.

Eighteen of the 25 patients were 72 percent developed, 182 plus or minus 11 percent dilation of the esophagus over an average follow-up of 21 months. Preoperative esophageal diameter is 22 millimeters and postoperative diameter was reevaluated at 33 millimeters.

In terms of the size, zero to 130 percent in green of seven patients, 130 to 150 percent in seven patients, 150 to 180 percent of normal in four patients and 180 percent plus in seven patients.

This is another example of a 3.2 centimeter dilated esophagus of a band. The same patient subsequently, where now you're already getting an S-shaped curve of the esophagus and a concern that this could lead to a pseudo-achalasia. Then this is after this patient was converted to gastric bypass. There is still a dilation of the esophagus above the band five months after conversion to gastric bypass.

Thirteen of these 18 patients with esophageal dilation were significant with dysphagia, vomiting or reflux symptoms. Eighteen of the 25 patients in the study had a nuance set of symptoms; seven patients remained asymptomatic, in spite of having a dilated esophagus.

Now, in terms of weight loss in these patients, our average preoperative body mass index was 44; our eligibility for surgery is a body mass index of 35 or

greater with comorbidity. I must say that, I am a strong advocate of the surgical treatment of obesity and have been for 20 years. In our program, we have done randomized prospective trials, comparing vertical banded gastroplasty to gastric bypass and so forth. So, I think it is important to have an effective and safe procedure for these patients.

The average body mass index only decreased to 39 after 22 months average follow-up. Average weight loss was 40 pounds, which you might think is a lot. The average assessed body weight loss was only 28 percent, which when we compare it to an equivalent group of patients who underwent gastric bypass who were matched for preoperative weight, age, sex and race, the percentage of excess weight loss in the LAP-BAND was 36 percent and then 74 percent in the column on your right for gastric bypass, a much, much more effective procedure.

Five of these patients with the esophageal dilation have had their bands removed. Three of the five bands were removed 30 to 42 months postoperatively. Two had their bands removed for weight loss. Four additional patients desired band removal for reasons of poor weight loss and worsening gastro-esophageal symptoms. We have had nine other patients down below who have had their bands removed and were not included in the analysis due to unavailable or uninterpretable preoperative upper GI film.

So, a total of 14 patients have had their bands removed of the 37 patients who have had it placed, about a third. We anticipate another five patients will have their bands removed because of inadequate weight loss.

In terms of what happens if you take the fluid out of the band, one of the patients did have a reduction in esophageal diameter. One of the patients did not.

The thing is, we have had two really successful patients like the ones you've heard today out of the 37. That is a very, very small percentage. We don't know what the significance of these findings are, but we think that it is very important that this be followed for more than two years; that all patients be followed for at least three years.

As I have mentioned, we have had five patients lost to follow-up. We have no idea what is going to happen to their esophagus. You have heard about the patient of Dr. Kuzmak's who went to Dr. Martin, who was lost to follow-up, with a massively dilated esophagus.

Now, these are the centers that have tried the use of the LAP-BAND and four of these centers are no longer doing this. We are no longer--we stopped doing the LAP-BAND two years ago. Mount Sinai is no longer doing it, probably because Dr. Greenstein is not there anymore. Dr. Ganier [ph] who is following those patients is taking out somewhere

between a third and 40 percent of the bands.

The group in San Diego, Drs. Wickgrove and Clark stopped doing this operation two years ago. The University of Iowa no longer does it. So, I am very concerned about the safety and efficacy of this procedure and its premature release at this point in time.

DR. KALLOO: Thank you, Dr. Sugarman.

MS. CORNELIUS: I would like to read into the record the following letter from Cynthia Jones of Dallas, Texas.

As of February, 1999, I had officially given up on my weight. I had tried everything from pills to having injections of pregnant mare's urine. Nothing worked. I had gotten so big that my life had become miserable. I figured that I was meant to be fat and would die by the time I was 50.

Out of the blue, my sister called and suggested the gastric banding procedure. My surgery was March 29, 1999. I was 300 pounds.

Today, I am 125 pounds lighter and have just completed my breast reduction surgery. I have about 40 pounds to go.

My whole life has changed. Not only am I healthier, but I am actually enjoying life. I have self-respect. My life is just beginning. I've always

dreamed of getting married and having children. That dream has now become a reality. For the first time in my life, men notice me.

I have no physical problems from surgery. The gastric banding has given me a second chance. I hope to keep this band forever. Please legalize this surgery so that other obese people can have a chance to begin anew.

DR. KALLOO: Okay, we are going to break for ten minutes exactly and then we will return promptly.

[Recess]

DR. KALLOO: I'd like to call to order the Open Committee Discussion session of this meeting. I would ask at this time that, all persons addressing the panel, come forward to the microphone and speak clearly, as the transcriptionist is dependent on this means of providing an accurate transcription of the proceedings of the meeting.

Before making your presentation to the panel, state your name and affiliation and the nature of your financial interest in that company, including whether or not travel was reimbursed.

Let me quickly remind you that, the definition of financial interest in the sponsor company may include compensation for time and services of clinical investigators, their assistants and staff, in conducting the

study and in appearing at the panel meeting on behalf of the applicant, a direct stake in the product under review, such as, inventor of the product, patent holder, owner of shares of stock, et cetera, owner or part owner of the company.

Of course, no statement is necessary from employees of that company.

I would ask that all persons addressing the panel come forward to the microphone and speak clearly, again. I would like to remind the panel that, they may ask for clarification of any points included in the sponsor's presentation, but discussion should not go beyond clarification.

The first speaker, as listed on the agenda, is Ellen Duke from BioEnterics Corporation.

PRESENTATION OF

ELLEN DUKE, DIRECTOR OF CLINICAL RESEARCH

BIOENTERICS CORPORATION

MS. DUKE: Good morning. My name is Ellen Duke. As President and Chief Executive Officer of BioEnterics Corporation, a subsidiary of InterMed (ph) Corporation, it is my privilege to produce a summary of information provided in our premarket approval application on the LAP-BAND adjustable gastric banding system.

After my presentation, Dr. David Munjal, our Director of Clinical Research and Regulatory Affairs will

describe the design of the U.S. study.

We are honored that Dr. Kenneth MacDonald, Chief of Gastrointestinal Surgery and Surgical Endoscopy and Professor of East Carolina School of Medicine will be presenting the pivotal U.S. study results and the risk-benefit analysis. Dr. MacDonald has implanted over 40 LAP-BAND systems during his participation in the original U.S. clinical study and the expanded and continuing access study.

Dr. MacDonald has been treating severely obese patients for over 15 years and has researched and published on the effects of the VC surgery on his patients. He has been very active in the American Society for Bariatrics Surgery and was elected to serve as President of the ASBS in 1996.

We also appreciate Professor Paul O'Brien's willingness to travel far from home to present the international study data. After participating in important studies in other obesity procedures, since 1994 Professor O'Brien has implanted over 700 LAP-BAND systems. Professor O'Brien is Professor of Surgery and Chairman of the Department of Surgery for Monash University and Alfred Hospital in Melbourne. He is President of the Obesity Surgery Society of Australia and New Zealand and has authored or co-authored over 100 papers on gastroenterology and surgical topics.

I will move as quickly through a brief history, a summary of preclinical testing, the literature review and literature meta-analysis.

In the mid-1980s, Dr. Kuzmak initiated use of an adjustable silicon gastric band, the ASGB. After obtaining rights to the device in 1989, in 1991 Intermed Development received FDA approval for an IDE for the ASGB. BioEnterics Corporation was established in 1991 to focus in the area of obesity and general surgery. The decision was made to develop a design more suitable for laparoscopic placement.

The new LAP-BAND, the adjustable gastric banding system increased the postoperative adjustability of the original design and eliminated the need to size, trim and suture the device closed during the procedure. This reduced the variability in the procedure and removed the sharp edges created when the ASGB was cut.

In September of 1993, the LAP-BAND system was first used clinically in Europe. The first international workshop on the use of the LAP-BAND system was held in 1994. In 1995, BioEnteric's IDE for a prospective clinical study was approved by the FDA and, in 1997, BioEnterics CE-marked the LAP-BAND system.

In 1998, U.S. study enrollment was completed. BioEnterics approached the FDA with a plan to combine the results of the U.S. study with information from a

retrospective, multicenters international clinical study and the FDA agreed.

The LAP-BAND system has been introduced gradually around the world since 1993, providing over six years of experience. Regulatory approval has been received and distribution initiated in more than 40 countries. Over 40,000 LAP-BAND systems have been used. There are over 250 publications describing LAP-BAND system experience in the medical literature.

Although there are other adjustable bands on the international market, these bands have very different designs and are not available in the United States. This is a picture of the band and the access port. You can see how the device is designed with a buckle closure and how the catheter passes through the buckle to the access port.

The band itself is silicon elastomer and has an inflatable inner shell. It has a buckle closure and silicon tubing connects the band to an access port placed outside the abdominal cavity. This access port is a standard design commonly used for chemotherapy.

A calibration tube which has a small balloon on the end is inflated in the stomach to assist in identification of the dissection points for the gastric pouch. Postoperatively, the inner diameter of the band can be adjusted by adding or withdrawing saline through the

access port.

Testing was performed to evaluate all levels of the manufacturing process, the raw materials and components from which the device is assembled, as well as finished devices, biocompatibility, the device's packaging, the sterilization process of the device and product shelf life. The results of these tests demonstrated that the product meets design and intended use specifications.

A problem with leakages at the access port tubing connection was identified through product surveillance and after a redesign, testing demonstrated several fold increase in fatigue resistance. In addition, during the final stages of development, the feasibility of laparoscopic placement of the device was evaluated.

This is the problem that brings us here today, obesity. Chronic obesity and, especially severe obesity has been recognized as a disease with serious health consequences. In simple terms, obesity is the result of an imbalance between caloric intake and the body's use of those calories, resulting from genetic, behavioral and environmental factors.

Degrees of obesity are commonly categorized using body mass index or BMI, which is weight in kilograms divided by height in meters squared. However you define it, obesity is a major health problem in the United States. An estimate

of the prevalence of obesity in our country is shown here. Fewer than half of American adults are within the normal weight category. More than a third fall into the categories in which negative health consequences have been demonstrated.

Over 11 million adults fall into the category of severe or morbid obesity. The impact on health of obesity is very serious. As you can see in this list, the comorbidities resulting from severe obesity. This includes major comorbidities that impact the longevity as well as quality of life.

Obesity increases the risk of death, which starts changing at about 27 BMI, doubles by 38 BMI and dramatically increases thereafter. The risk of most comorbidities show similar curves. For these people, the combination of genetic predisposition and the behavioral and environmental attributes of our culture have combined to create a truly toxic situation. You will see that the mean BMI of the participants in the U.S. clinical study was literally off the chart.

The international subjects had a BMI of 43 and the U.S. subjects had a BMI average of 47, indicating a very high mortality risk.

It is estimated that the annual adult deaths attributable to obesity is almost 300,000, rivaling tobacco

as a leading preventable cause of death in the United States.

Beside the personal health risks, premature death and suffering associated with obesity, this disease is a financial drain on individuals and our society. As you can see, obesity-related health costs are huge and increasing, despite significant investments in research. Although billions of dollars are spent every year on dietary programs and medications, the evidence is overwhelming that current medical therapy alone is limited in its effectiveness.

It has been shown that a weight loss of just ten percent is effective in improving comorbidities. The NIH estimates that only five percent of severely obese patients can be successfully treated medically because although severely obese patients can lose weight as well as anyone else, the weight returns.

Ten NIH consensus conferences have recognized that only surgery is able to provide the severely obese patient with sustained weight loss.

If you think this looks like one of my previous slides, you're right. Current data demonstrates that almost all of these conditions are improved or even cured by weight loss. Surgical weight loss improves health.

With the valuable assistance of many surgeons BioEnterics has provided substantial evidence of the safety

and efficacy of the LAP-BAND system and its relationship to the alternative procedures. We will move quickly the literature review and meta-analysis to the important U.S. prospective clinical study and international retrospective study information.

To evaluate the efficacy and safety information regarding the two most common bariatrics surgery procedures in the United States, the gastric bypass and vertical banding gastroplasty, also known as VBG, as well as the LAP-BAND system, a literature review was conducted. More than a thousand publications were reviewed.

This is a simple drawing of the (?) gastric bypass, which is probably the most common obesity surgery performed in the United States. It is typically performed as an open procedure, although some surgeons are able to do this laparoscopically. This is considered a good operation that combines restriction with a malabsorptive component. Bypass patients typically experience greater weight loss than patients with purely restrictive procedures due to the malabsorption and dumping.

Dumping is a gastrointestinal distress that a patient experiences upon eating sweets. The sweet sensitivity encourages patients to eat a diet low in simple carbohydrates. However, gastric bypass surgery is considered invasive, even when performed laparoscopically

and this has impeded widespread acceptance by patients.

This is a simple drawing the VBG, which is also commonly performed in the United States. It is usually performed as an open procedure. The band is made by the surgeon, typically a Marlex mesh or silicon tubing. With no malabsorptive component, the weight loss is not as great as that for the bypass, but has been shown to improve comorbidities.

The American Obesity Association and Shape Up, America have provided an guidance for treatment of adult obesity, which includes this table regarding the results of the bypass and VBG. As you can see, both result in significant weight loss, which is greater with the gastric bypass. Although this review did not provide bypass reoperation, as it did for the VBG, this is generally accepted to be around ten percent.

As a significant percentage of these patients are women, the guidance notes a concern regarding the effects of these nutritional deficiencies during pregnancy, requiring careful monitoring and supplementation.

The ASBS estimates that, only 30,000 of these procedures, 30,000 are being done each year. That means that only a handful of every thousand who need it are getting surgery, the only treatment that has been demonstrated to be effective. The LAP-BAND system was

designed to enable and adjustable weight loss procedure, with less operative mortality and serious morbidity and to avoid the nutritional deficiencies.

This is a drawing the LAP-BAND system in place. It is almost always performed laparoscopically. The band is placed around the top of the stomach to form a small gastric pouch, to restrict the amount of food that can be consumed. As shown in the inset, gastro-gastric sutures hold the band in place anteriorly. Some surgeons now place a retro gastric suture or take a slightly different approach to reduce the most common problem of the procedure, band slippage.

The procedure is less invasive than the alternative procedures, even when performed as an open procedure. It's adjustability provides advantages by allowing a customization of weight loss to the patient's needs, for example, in pregnancy to reduce discomfort and provide additional nutrition.

Unlike the VBG or gastric bypass, this procedure has been demonstrated to relatively easy to revise or reverse and this can usually be done laparoscopically.

The meta-analysis of the published surgical literature provides a statistical comparison between the two most commonly performed U.S. procedures and the LAP-BAND system, including weight loss, morbidity and mortality.

This provides important information regarding relative differences between procedures, an opportunity to compare apples to apples which, of course, cannot be done when comparing literature results to those of a multicenter clinical study, for example, as morbidity is also underreported.

All procedures show significant sustained weight loss. Peri-operative mortality and morbidity with a LAP-BAND system was significantly less than with the other procedures. The details provided in the submission show the reductions in individual peri-operative risks.

Looking at relative differences postoperatively, the LAP-BAND system reduces vomiting relative to the VBG, while avoiding the nutritional deficiencies reported with bypass. With the LAP-BAND, the problem of staple line dehiscence has been eliminated and incisional hernias nearly so. The risk of stomal obstructions is reduced.

Band pouch slippage is the most frequent postoperative complication of the LAP-BAND system. Taken as a whole, the meta-analysis demonstrates significant weight loss, significantly reduced peri-operative morbidity and mortality as well as reduced incidence and seriousness of postoperative morbidity with the LAP-BAND system.

So, what can we conclude from this literature review and this analysis?

First, that the gastric bypass is a good procedure. It results in the best weight loss and has the lowest rate of reoperation, but it is invasive and includes risk of nutritional deficiencies. The VBG produces good weight loss, although not as much as with the bypass, but the nutritional deficiencies of the bypass are avoided. Finally, that the LAP-BAND system produces good weight loss, has the least operative morbidity and mortality, is adjustable and when necessary, is the easiest to revise or reverse.

The literature review and meta-analysis provide substantial evidence of the safety and effectiveness of the LAP-BAND system.

Now, Dr. David Munjal, our Director of Clinical Research will discuss the clinical study design.

[Pause]

PRESENTATION OF

DAVID MUNJAL, M. D., PH.D., RAC

DIRECTOR OF CLINICAL RESEARCH AND RA

DR. MUNJAL: Mr. Chairman, members of the Advisory Panel, ladies and gentlemen, good morning.

My name is David Munjal. It is indeed a privilege to present to you this morning an overview of the BioEnterics U.S. clinical study design.

The clinical study was initiated and conducted

under an IDE approved by the FDA in April of 1995. The first patient was enrolled on June 13, 1995 and the patient and government was completed on June 22, 1998.

The eligibility criteria for patients to receive the LAP-BAND system are listed here. It must be emphasized that the LAP-BAND system is indicated for use only in severely obese adult patients with a BMI of equal or greater than 40 or with a BMI of equal or greater than 35 with one or more comorbid conditions.

The patients are greater than 100 pounds over their ideal weight and have failed more conservative weight reduction alternatives, such as, supervised diet, exercise and behavior modification programs. Patients who elect to have the surgery must make the commitment to accept significant changes in their eating habits for the rest of their lives.

This multicenter, single arm prospective clinical investigation was undertaken to evaluate the safety and efficacy of the LAP-BAND system. As indicated, each subject served as his or her own control. That is, the subject's postoperative weight at different times was compared to the preoperative weight. Similarly, the postoperative quality of life parameters were compared with the preoperative values.

Eight institutions geographically distributed

throughout the United States participated in this study. The locations as well as principle investigator names and the site involvement are shown here. A total of 299 subjects were enrolled in the study.

I would like to make a comment here that, no investigator has formally withdrawn from this study. Two investigators, Dr. Doharty in Iowa and Dr. Martin in New Orleans, there was a mutual decision made to stop the enrollment of the patients due to their other commitments and having reached more than enough patients in those centers.

In addition, Dr. Robert Greenstein resigned and left Mount Sinai Hospital. So, Dr. Gonye [ph] is continuing and following the patients while Dr. Kuzmak, due to health reasons, took retirement. I want to assure the panel here that all the patients, 299, which are part of this study, are being followed for the safety and efficacy of these patients.

This slide gives the inclusion criteria. Subjects were to be included in this study only if they met listed criteria, the principal criteria, of course, being a BMI of equal or greater than 40, 100 pounds above ideal weight.

This slide provides the exclusion criteria. Subjects were excluded from entry into the study if any of the following listed conditions were present.

The primary efficacy endpoint was percent excess weight loss. The secondary efficacy endpoints were: change in weight loss, BMI and quality of life, which included the Beck Depression Index, multidimensional body cell (?)-ations, and RAND-36. The efficacy outcomes were analyzed by constructing 95 percent confidence intervals and comparing results with historical studies of gastric bypass and vertical valid gastroplasty, two common bariatric surgery procedures, commonly being used in the United States.

A goal of 50 percent excess weight loss was discussed with the FDA and incorporated into the study design at the initiation of the trial in lieu of a specific study hypothesis. This goal was based on early literature, on the vertical banded gastroplasty and the recognized health benefits of weight loss.

However, recent published literature has demonstrated that the substantial benefits can be achieved with modest weight loss.

Safety was measured by the incidence and severity of operative and postoperative complications and by the performance of all components and accessories.

So, Mr. Chairman, I thank you very much for paying attention and now it is my privilege to invite Dr.Kenneth MacDonald from East Carolina University to talk about the safety and efficacy of the U.S. clinical study.

Thank you.

PRESENTATION OF

KENNETH G. MacDONALD, JR., M. D.

EAST CAROLINA UNIVERSITY

DR. MacDONALD: Good morning.

My name is Ken MacDonald. As of ten days, I will be promoted to Professor of Surgery at East Carolina University. So, I'm happy about that.

My trip to this meeting was paid for by BioEnterics. I have been reimbursed for time spent. I do not own stock in the company nor do I have any other financial interests. I was one of the investigators in the U.S. clinical studies and BioEnterics did also provide a research coordinator to my university. I was asked to present the safety and efficacy from the U.S. clinical study on the LAP-BAND.

Other than for the LAP-BAND trial, my background is with a long experience with gastric bypass. I also performed vertical banded gastroplasty for a couple of years in a comparative study at our institution.

Slide, please.

This describes the demographics of the U.S. study patients, age range, from 18 to 56 years old, with a mean of 39 years. Eighty-five percent were female, common were the most serious bariatric operations, and the racial

distribution is shown here, with 80 percent caucasian.

The U.S. study patients met the criteria for morbid obesity, with a mean weight of 293 pounds, a mean excess weight of 156 pounds. The BMI ranged from 36 to a high of 74, with a mean of 47.7. Significantly, 28 percent of the patients had a BMI of greater than 50 and, therefore, were defined as super obese.

This lists the preoperative comorbidities of the U.S. study patients. Forty-two percent had hypertension. Twenty-five percent had gallstones and 16 percent each had asthma and diabetes, again, common with most morbidly obese populations.

This slide shows the mean weight gain of the patients in the U.S. study during the years preceding placement of the LAP-BAND. During the five years before surgery, despite dieting by many, the patients gained a mean of 54 pounds. In the 12 months before surgery, they gained a mean of 17 pounds. This just emphasizes that obesity is a progressive disease where the patients generally continue to gain weight over time, despite dieting.

This, again, is data from the U.S. study patients' history showing a phenomenon common with the morbidly obese. During each year prior to surgery, the group lost around 30 pounds in each group with medical weight loss programs. Only two subsequently regained more weight than they had

originally lost, usually within five to seven months after their diet ended.

This shows the distribution of the patients, which I'm going to try to explain so we can understand. Starting with 299, all of whom were used in the safety analysis, subtracting seven patients who were revised from a previous open, adjustable silicon gastric banding operation, this left 292 patients that were used in the efficacy analysis.

Now, these 259 were completed laparoscopically and 33 by open surgery. Of this open group, 20 were scheduled-- I mean there were 20 performed open; 19 were at one site. Dr. Kuzmak's center, who did not perform laparoscopic surgery. Thirteen of the open operations were begun as a planned laparoscopic procedure which resulted in a conversion of 4.7 percent, which I believe is quite good for a new laparoscopic procedure.

This describes the accountability in the U.S. study, showing the number of patients expected at each time interval, compared to the number in the active column on which data was available at or subsequent to the given follow-up visit. For our analysis today, we will concentrate on the 24-month group, which we had data on 215 patients from 24 months or more, giving an accountability of 88 percent.

This describes the analysis groups in another way

in the U.S. study. As you saw in the material presented to you, safety analysis was performed on all 299 patients. For the efficacy analysis, we took off the seven ASGB conversions, leaving 292 patients.

Four patients were explanted or meaning the band was taken out before the first follow-up visit at three weeks. So, this left 288 patients in the intent to treat group. The group we are going to talk about primarily today are the 175 patients who had data right at their 24-month visit and then we had data on 212 patients from 24 months on.

Now, the analysis for all three of these groups are provided in the PMA. I'll mention the day and the results are very similar for all three groups. I hope that is not too confusing.

I'll next present the efficacy data from the U.S. study. This shows the weight loss at various time intervals after surgery, reaching a maximum of 55 pounds and 38 percent of excess weight at two years. The mean BMI fell from 47 preoperatively to a low of 38 at two years. These results, as you can see, remained pretty stable on out to 36 months of follow-up, with no significant weight regained.

This is a bar graph showing weight loss as a mean percent of excess weight lost, which is standard at different time intervals, reaching again a maximum loss of

38 percent of the excess weight at 24 months, with quite stable loss from 12 to 36 months postop.

This shows the falling BMI after placement of the LAP-BAND, again, starting with a mean of 47 preop and gradually decreasing to a minimum of 38 at 24 months after surgery. Again, no significant change from 12 to 36 months.

This chart shows the percentages of each group that lost greater than 25 percent, greater than 33 percent and greater than 50 percent of excess weight. At 24 months, 73 percent of the group lost greater than 25 percent of their excess weight. Approximately one half of 53 percent lost greater than 33 percent of their excess weight. About one quarter or 26 percent lost greater than 50 percent of their excess weight.

Again, note that these changes did not change much from 24 to 36 months postop.

This shows the percentage of patients in each time group with a BMI of less than 40. Nine percent of the 292 initial patients in the efficacy group had a BMI of less than 40. Many of these met alternative criteria of greater than a hundred pounds over ideal body weight, with a comorbidity. By two years, 64 percent of these 175 of whom we had data right at two years, had a BMI of less than 40. This was not significantly different from the 60 percent of the group at three years.

This bar graph shows the percentage of patients at each time interval that had a BMI of greater than 50, which again defines super obesity. This fell from 30 percent of the original group down to six percent of the 175 patients at two-years follow-up, which is a highly significant decrease. This number was quite stable on out to three years.

Now, like I have mentioned, this demonstrates the similarity of the different analysis groups, the analysis group of 175 patients with data at the 24-month visit and the 212 with data from 24 to 36 months and the entire intent to treat group with 288 patients. There are no significant differences between any of these three groups in terms of percent excess weight loss, mean weight and mean BMI.

This slide shows the patients with higher BMIs. As you can see in this column, lost less percent of their excess weight. It ranges from 48 percent in this BMI group to only 34 percent of the 50-plus BMI group, although the heavier patients lost more weight, 48 pounds and 72 pounds.

This is a recognized phenomenon with other gastric restrictive operations. We just mention it because it does affect the analysis.

I'll move next to quality of life data. The quality of life is measured by three validated instruments to evaluate depression, appearance and mental and physical

health. They all showed a highly significant improvement from baseline before surgery to 12 months after surgery.

This is a graphic representation of the RAND-36 subscales, which is one of the tests which are oriented in a radial direction with the baseline or preop results plotted along each one of these axes. Now, to describe simply the higher the number--in all cases, going in that direction--the better the response. This measures things like roll limit, energy, fatigue, emotional well-being, et cetera.

This shows a significant improvement in all the subscales at 12 months, plotted in blue, just to give you an idea of the degree of improvement in these measurements.

This is a bar graph of answers to specific questions on the RAND-36, showing the improvement in severe limitation of activity, from preop to 12 months after band placement. Now, dramatic improvements were seen in things like vigorous activities, climbing several flights of stairs, walking more than a mile and even walking several blocks, all showing greater than twofold improvement.

Now, to the safety results of the study. This shows the adverse events. We have tried to look at this in many different ways. So, I'll try to get through all this.

This was reported with a frequency of greater than ten percent. Most of these were of low severity and not very clinically important. It is also important to mention

that any single event may have been reported in more than one category.

For example, gastric slippage, also often caused stoma obstruction and the symptoms of nausea, vomiting and GU reflux. So, one event may have been reported as all these symptoms by the investigator. A single event could be counted in both the peri-op, which was less than three weeks and the postop, which is greater than a three-week period and the total percentage, therefore, is not always the sum of the two groups. So, don't add all these up, because you might find some disparities.

The most important event in this slide is the gastric slippage and the pouch dilation problem, which occurred in 23 percent or 22 in some analyses of the total patients, usually greater than three weeks after surgery and very few of them in the immediate peri-op period.

Now, this could occur when the posterior wall of the stomach was not fixed by natural adhesions, allowing the stomach to herniate up through the band, causing the pouch to enlarge. In some cases, frequent cases resulted in obstruction of the outlet. I'm going to spend some time later discussing this.

Simple stoma obstruction could be caused by just simply putting too much saline in the band and be treated just by taking some out in radiology. In some cases it

could be due to this more serious slippage problem.

This shows the adverse events that were reported with a frequency of five to nine percent. Again, many of these were very non-specific, with a questionable relationship to the band, like diarrhea and constipation. Many were mild and self-limited.

This is a continuation of the five to nine percent adverse events. The significant ones here related to the band include the esophageal dilation problem, detailed nicely by Dr. Sugarman. This had a frequency of six percent in the total series.

Now, to present another opinion, many of us felt this was a transient and insignificant event, which is just noted on swallows. Since you have a degree of obstruction by the band just below the junction of esophagus and the stomach, the esophagus would dilate up as the barium column passed down and then go back to normal when it passed out of the pouch. Obviously, it might not do that in all cases.

Port displacement occurred in five percent, here, where the access port implanted under the director sheet twisted or moved in a way to cause problems after surgery to adjust the band.

Now, these were the definitions that were used to rate the severity of the adverse events by the investigators. Mild to moderate, as you can see and severe,

which was defined as incapacitating with ability to work or do usual activity. The definition of serious for this study included, obviously, life-threatening and fatal. The most common reason that an event was labeled as serious were these two, requiring hospitalization greater than 24 hours and prolonging hospitalization.

So, anything like a fever or a headache in one case, could prolong hospitalization and, thus, be termed as serious. Other things that were used were unexpected events.

Now, 29 percent of the subjects had events that were defined as severe. Thirty-six percent had events defined as serious. There was considerable overlap though with 41 percent of patients having either a severe or serious adverse event. I will discuss how these events break down in terms of these definitions of severity.

This slide shows how adverse events with a frequency of greater than ten person--the slide you saw previously--were rated in terms of severity by the investigators. While nausea and vomiting was extremely common, it was felt to be severe in only two percent of the patients, the same for reflux.

Slippage was felt to be severe in eight percent of the patients. I'm going to detail this a little bit more with how they were treated. Again, many events would be

reported with a single occurrence as slippage. It would also cause reflux, nausea and vomiting and stoma obstruction. Stoma obstruction was rated as severe in five percent of the patients.

These are the events with lower frequency, from five to nine percent, rated according to severity. The severe column is bold. Those I would consider significant and related to the device would include dysphasia, difficulty swallowing, port site pain and incisional infection, all ranked as severe in one percent or less.

Important events here include esophageal dilation problems, ranked as, rated as severe in two percent, port displacement, severe in one percent and incisional pain, down there, less than one percent.

These are important adverse events that didn't get mentioned in some of the other graphs because they occurred more infrequently, but they certainly deserve mentioning because of their severity and the specific relationship to the band.

There were three gastric perforation during placement of the band. Two were discovered during the operation and repaired. One occurred during a band revision and was treat by percutaneous strainage. There was one esophageal perforation, requiring removal of the band on the first day after surgery, which had no ultimate adverse

sequelae.

There were three band erosions into the stomach, occurring in one percent of the patients. Two of these followed the operative gastric perforations, which were discussed here. These events did not result in serious infection or leakage. It sounds severe, but they don't usually cause us problems. They can be treated with laparoscopic removal of the band in all cases.

There were seven leaks from the access port tubing, requiring replacement of the access port. These occurred at the tubing, the port connection, which actually resulted in a design change of the device. Hopefully, it will resolve that problem.

This is a review of the important adverse events which, again, were ranked as serious by the investigators. Band slippage was felt to be severe in 35 or 12 percent, usually because it caused a hospitalization of greater than 24 hours or prolonged the hospitalization. For similar reasons, eight percent of stoma obstructions were ranked as serious.

Gastric esophageal reflux, esophageal dilatation, erosion and GI perforation were all ranked as serious in one percent each.

This shows the rate of adverse events, plotted as event per patient year. There are two important points

here. Adverse events per patient declined progressively in each year after implantation. Those events which were ranked as serious by the investigators were a very small percentage of the total and also progressively decreased with time after surgery.

Well, not shown on this side is, there have been no new types of adverse events appearing later in the follow-up.

There was no peri-operative mortality. One death in the U.S. study occurred one week after laparoscopic explantation of the band due to patient request. This was 16 months after initial placement and the death was ruled as due to mixed drug intoxication. As Dr. Martin already discussed, we recently learned of another mortality occurring about four weeks ago, find a revision to a gastric bypass operation that occurred one day after the operation. The patient was 42 months after initial placement of the band and six months after completion of the study at 36 months.

DR. SAWICKI: What was the cause?

DR. MARTIN: It's pending a coroner's review because unfortunately the coroner went on vacation the day after the autopsy.

DR. MacDONALD: Thank you.

This still details the management of the 66 band

slippages, which represents 22 percent of the 299 patients. Sixteen percent of these slippages or 24 percent of this group were managed by simple stoma adjustment, with withdrawal of saline from the band. Twenty-six percent of these cases or 17 patients were managed by operative revision or replacement of the band, often times performed laparoscopically. Nineteen of the slippages or 29 percent of the total were managed by explant or removal of the band which, again, could be performed laparoscopically in most cases.

The decision to revise, replace or explant the band was very dependent, as you will see, on surgeon comfort and experience. While patient preference occasionally may have influenced his decision, this would be highly dependent on the way the surgeon counseled the patient.

Some slippages did not have concomitant obstruction and no action was taken. Nine percent were listed as ongoing, with or without symptoms and the management was not recorded in six cases, six percent.

Revision operations were performed in 22 patients, as already has been alluded to or seven percent of the initial group of 299 patients. In eight patients the band was removed, with replacement of a new band. Six of these were able to be performed laparoscopically. Two were removed and later replaced with new bands by open surgery at

a later date due to patient wishes. The existing band was revised without removal in 12 cases and this was performed laparoscopically in three and open in nine.

The method of management, again, was highly dependent on surgeon experience and preference. It is significant that 41 percent of these more complicated revision operations could be performed laparoscopically, although it was early in the learning curve with this procedure in the United States.

Now, 48 of the original 299 bands or 16 percent were also removed for various reasons, called explants. This, again, was investigator-dependent as over one half occurred in two of the centers. Twenty of the 48 were able to be removed laparoscopically. Three of these patients had a concomitant gastric bypass operation. Twenty-eight were removed by open surgery and 16 of these had an alternative gastric restrictive operation.

This slide shows the break down of the 48 explants by site. Again, 25 patients occurred in two centers and these were the centers with the most patients and who had started earlier than most others. Two other centers had lower numbers, but very significant percentage of explants in their groups. You can see, the other four centers had much lower rates of explantation.

These are possible reasons to explain why explants

or conversions occurred more frequently in some than others. Surgeon bias, particularly combined with a lack of experience with management of patients with this band was probably a major factor leading to the decision to abandon the band in favor of an operation that they are more familiar with, which is understandable.

Other reasons facilitating reoperations with this procedure would include the ease of either explantation or conversion, as well as just being able to perform it laparoscopically, which undoubtedly influenced the decision making of surgeons who were dealing with an unfamiliar operation. If it is easy to do it, you might be inclined to do it faster or sooner.

The conclusions from the safety analysis are listed here. Band or gastric slippage was the primary device-related adverse event, with an instance of 22 percent. I personally expect that this will decrease with modification, appropriate modifications in technique.

There was no device-related mortality in this high risk group of patients, even though, again, it was early in the learning curve for all of these surgeons in the United States. The operation was easily performed laparoscopically. There was a low risk of serious peri-operative, less than three weeks, complication.

Very importantly and not alluded to much, is the

degree of restriction may be adjusted without surgery. This is a major advantage of the device. Revisions or reversals may be performed with low morbidity, often times laparoscopically.

Now, I'd like to introduce Dr. Paul O'Brien from--

DR. KALLOO: Before you go, may I have a brief clarification?

DR. MacDONALD: Yes, sir.

DR. KALLOO: What fraction of patients had gotten to a BMI of 27 by 24 months? I chose 27 because it was quoted in an earlier presentation by--

DR. MacDONALD: May I see that slide?

[Pause]

DR. MacDONALD: Okay, I'm sorry. What was your question again?

DR. KALLOO: What fraction of patients got to a BMI of 27 or less by 24 months?

DR. MacDONALD: To a BMI of 27 or less?

DR. KALLOO: Or less, yes.

[Pause]

DR. MacDONALD: Can anybody help me with that data? I don't recall from where I presented. I'll try to answer that for you.

DR. KALLOO: I chose 27 specifically because it was quoted as the BMI above which complications from obesity

significantly--

DR. MacDONALD: Subject to your normal BMI at 24 months, 6.9 percent reached BMI less than 27 in the U.S. study and 12.5 percent in the international.

DR. KALLOO: Thank you.

DR. MacDONALD: Thank you.

DR. SAWICKI: I have one clarification question.

DR. MacDONALD: Yes, sir.

DR. SAWICKI: Can you tell me--because your data is broken down--the number or percentage of patients who had the band placed that required a reoperation?

DR. KALLOO: Could you repeat the question into the microphone?

DR. SAWICKI: The number or percentage of patients in the study who required reoperation for whatever reason.

DR. MacDONALD: Do we have that total figure on a slide?

DR. SAWICKI: The total.

[Pause]

DR. MacDONALD: I know we do, if it can be found.

[Pause]

DR. MacDONALD: Well, I'll try to tell you. Let's see, revisions were seven percent of the initial group, explants in 16 percent. So, that's combined. That's 23 percent. I would say, just to try and give you an educated

guess until we can find definite slides, somewhere between 27 and 33 percent.

DR. KALLOO: I'm sorry, one last question.

Do you have a breakdown of complications by site?

[Pause]

DR. MacDONALD: What's that; what percentage was that?

DR. SAWICKI: Seventy out of 292?

DR. MacDONALD: That data would be available, but I don't recall having seen it classified that way.

DR. NELSON: A quick question. There's a sizable loss of follow-up down from 300 patients to 175. Are your results calculated on just the ones you were able to follow-up. Secondly, why do you think they were--what is the reduction from 299 to the previous slide, that 175 evaluable events at two years.

DR. MacDONALD: Okay, that relates to the accountability issue. That would have meant the people who were explanted, we knew what happened to them, even though they were not included in that number. It would include some that had not yet reached the two-year period.

Right at that--you know, 175 was patients that showed up at the 24-month visit, plus or minus three months. Obviously, everybody is not going to be that compliant. So, that is why we used another figure to calculate the same

results, the 24 on--you know, patients we had dated from 24 months and subsequent.

Then, of course, there would be a loss of follow-up where patients just simply did not return and you did not know what happened to them. I can probably give you that data, seven people out of the total group.

DR. NELSON: Do you know what percentage were lost to follow-up? I guess the main question is, what are the success results based on intention to treat and, in fact, dividing by everyone in the study or do you exclude those patients who don't follow up?

DR. MacDONALD: This is the patients who we had active, meaning data actually on it, on those patients. Again, out of 243 expected patients, we had data on 215. So, that is how the accountability of 88 percent was calculated. That failed because of time at 36 months down to only 78 percent.

I'd like to give you the exact percentage of loss to follow-up at each time interval if we have it. I don't know that off the top of my head though.

DR. KALLOO: Okay, why don't we continue with the presentations and at the end, if there are other questions, let's--also, I want to remind the audience that you have to be invited up to the podium to speak. So, please refrain from making comments.

PRESENTATION OF

PAUL O'BRIEN, M. D.,

PROFESSOR OF SURGERY, MONASH UNIVERSITY, AUSTRALIA

DR. O'BRIEN: Thank you.

My name is Paul O'Brien. I am Chairman of the Department of Surgery at Monash University in Melbourne and I'm the head of General Surgery at the Alfred Hospital in Melbourne.

The costs of my transport have been covered by BioEnterics. I do own stock in Intermed Corporation, which I bought on the open market. I am funded or my department is funded for the international retrospective and prospective studies, in which we are involved.

I am pleased to report to you the data regarding the international study. There were six centers around the world who contributed patients, one in Mexico, one in France, two in Belgium, one initially and my center in Melbourne. Generally, each unit contributed 75 patients to the study, with a total enrollment of 441 patients.

The objectives of the study were to measure weight loss during a five-year follow-up period after LAP-BAND placement, to measure adverse events during this follow-up period in the peri-operative phase and to measure changes in comorbid conditions.

The protocol that we followed was substantially

similar to the U.S. protocol. Significant differences, however, were first that, entry into the study only occurred after the surgeon had treated 50 patients. So, they were very much further down the learning curve than the investigators in the United States.

That included patients who had a body mass index in the range of 35 to 40, with associated comorbidities and because the study began in 1993, we had the opportunity for a longer follow-up. So, we have some four-year data available.

We measured comorbidity data at baseline and during follow-up.

Of the 441 patients, 97 percent were female, with a mean age of 34 years and 83 percent were caucasian. The mean weight in the study group was 257 pounds, which is less than the U.S. study, which had a mean weight of 293 pounds. The mean BMI was 43.

The vast majority of the cases were completed laparoscopically. There was conversion to open placement in 3.4 percent.

Of particular note is the very low incidence of peri-operative adverse events. Only six incidents were recorded of 1.4 percent. I'd just like to look at some of the factors which could be operative in this very low rate.

Firstly, we can recognize that there was a greater

experience by the international surgeons involved in this study because they began incorporating patients into this study after they had some experience. You also have to recognize a retrospective study. It is likely in this that, the mild or moderate adverse events would have been missed. The mechanism for identifying the adverse events in the peri-operative period was by an independent chart review, which would note particularly such matters as prolonged length of stay, readmission, reoperation, additional treatments.

In my own practice and in my own experience with more than 700 of these patients, I used a prospective method for collecting peri-operative adverse events, but I used the same criteria that were shown on the previous slide. Using those techniques, I have an adverse event rate of 1.2 percent. So, I feel that the 1.4 percent is a true reflection of the very low incidence of adverse events that occur in the peri-operative period with this LAP-BAND placement.

The more significance are the late events, which occur after placement. The most common is gastric prolapse or slippage, which occurred in 74 of these patients. Erosion of the LAP-BAND into the stomach has occurred in six patients. Tubing and band leaks have occurred in 44 patients.

Can I have that slide back, thanks?

The number of comments to be made about these data, firstly the high frequency of the prolapse and the addition of the erosions leads to reoperation. In 64 of the patients, this was done by revisional procedure and in 16 patients, there was explantation of the device. Generally, they were done laparoscopically and it has now become the standard to treat both problems laparoscopically.

The frequency is decreasing and as we saw with the U.S. study, the frequency of these problems are decreasing. Certainly, in my own experience, the figures that we see here of around 78 percent of prolapse is true for the earlier experience. This has become much less of a problem in later experience. In the last 300 patients that I have treated only two have come to any reoperation.

I think I need to comment also about the data that has been presented about esophageal dilatation. No episodes of esophageal dilatation were identified in this study. Apart from the dilatation that inevitable occurs when prolapse and then obstruction occurs, we don't see that problem of esophageal dilatation in my own experience.

We have many barium meals. We have done esophageal manometry before and at one year after operation in a number of patients. We have not identified any dismotility and we interpreted the data that has been

presented as representing a physiological change.

The weight loss which has occurred shows a particular pattern characteristic of LAP-BAND placement, with a gentle, steady rise in the percent of the excess weight lost, up to 50 percent in two years. Twelve months onwards, the weight has remained in the range of 45 to 50 percent and certainly in my experience, now after six years follow-up, I have stability of weight after the 24 month period.

A similar pattern can been seen with the change in body mass index from 43 and then stability over the last three years of the follow-up period.

Of particular importance in these patients is the change in comorbidity and of this selective data here from the more extensive in the PMA, have five diseases. We are looking now at the complete resolution of these diseases. We define complete resolution as the absence of any clinical syndrome of disease and the absence of treatment. In the case of diabetes, normal biochemistry. Forty percent of diabetics had complete resolution of the follow-up period. Twenty-two percent of hypertensive patients had normal blood pressure without treatment and more the half the patients with sleep apnea no longer had this problem.

There are also major benefits for osteoarthritis and for diseases of venous stasis.

In conclusion, in terms of safety, we find that the placement of the LAP-BAND is safe. It has a very low incidence of serious peri-operative morbidity and there's been no mortality in our study in the peri-operative phase and no mortality in the follow-up stage.

Revision or repair of tubing or removal of the device has been necessary in 28 percent of the patients, the most common problem being that of prolapse. These late problems are manageable, generally laparoscopically and there is strong reason to believe that they are decreasing markedly in incidence.

Next slide.

In terms of efficacy, we find that the LAP-BAND system leads to significant weight loss, in the range of 45 to 50 percent of weight loss. If this weight loss is sustained over four years, then it is associated with major reductions in comorbidity.

I'd like to hand on now back to Dr. Kenneth MacDonald, to talk about--

DR. KALLOO: I have a brief question before you proceed. You mentioned that there was an experience of about 50 patients before recruiting patients in this study. Do you have any data about the morbidity and mortality in that initial 50 or what I would call the learning curve?

DR. O'BRIEN: Not this part of the study. It

wasn't collected as part of the study. I have my own data and I certainly had more morbidity, more troubles in that early phase. That was early in the phase of learning about the procedure and how best to apply. Over the years, that knowledge has evolved.

So, even at 50 we were not, I think, at the level we are at now.

DR. KALLOO: Thank you.

DR. HIRSCH: Could you tell us--I'm sorry.

DR. KALLOO: Go ahead.

DR. HIRSCH: Could you tell us what the number of patients is that were available for observation at four years, from the starting, I guess, 441?

DR. O'BRIEN: Just say the question again. I don't quite understand what you're saying.

DR. HIRSCH: The study began with 441 subjects and you presented data on the four-year observation. I just wondered what the number--

DR. O'BRIEN: After four years, I'd have to get some advice from someone on that.

DR. HIRSCH: That's all right. Perhaps you can let us know later. I don't want to hold you.

DR. O'BRIEN: It's a relatively modest number, I should think.

DR. STEINBACH: Maybe I'm asking the same question

in a different way. What percentage of patients four years ago were lost to follow-up?

DR. HIRSCH: It's exactly the same question. So, maybe two of us are curious. Maybe we can get an answer.

DR. KALLOO: Why don't you come back later with that response.

Yes?

MS. CORNELIUS: You said 28 percent had revisions or whatever, repairs for prolapse. Did they go on to have a second time or what happens with that?

DR. O'BRIEN: I don't believe there are any second revisions beyond [simultaneous discussion] implantation.

MS. CORNELIUS: So, they have it once, one out of--

DR. O'BRIEN: Sixty-four had revisions as a one off. That is our experience. We have had very few who have needed further procedures after that. The prolapse tends not to recur once its treated because of the adhesions that are already in place.

DR. SAWICKI: I have one question. Can you come back to the issue of esophageal motility? You were talking about a number of patients that have presented with dilated esophograms basically and you thought it wasn't clinically significant.

Can you tell us roughly, ballpark, how many